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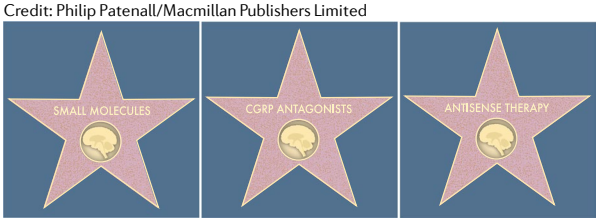

In the news

STARS OF NEUROLOGY MEET AT AAN 2018

Los Angeles provided the venue for this year's American Academy of Neurology Annual Meeting (AAN 2018). The programme featured presentations from big names and rising stars in the neurology field and highlighted an array of promising new therapies.

Advances in migraine treatment came under the spotlight at AAN 2018, with a particular focus on therapies that target calcitonin gene-related peptide (CGRP) — a neurotransmitter that is released from sensory neurons during migraine attacks. Joel Trugman reported on ACHIEVE I, a phase II trial of the CGRP receptor antagonist ubrogepant for the acute treatment of migraine. The drug provided significant benefits with regard to pain and migraine-associated symptoms.

Monoclonal antibodies against CGRP are also proving beneficial in individuals with migraine. Uwe Reuter presented evidence that erenumab can provide pain relief in patients with difficult-to-treat migraine. In addition, Richard Lipton reported that patients with chronic migraine experienced a significant reduction in monthly migraine days in response to treatment with eptinezumab (8.2-day reduction, compared with 5.6 days in placebo-treated patients).

Antisense oligonucleotide (ASO) therapy received top billing at AAN 2018. Sarah Tabrizi reported on a phase I/IIa trial of IONIS-HTT_{Rx} in patients with early-stage Huntington disease. The treatment was well tolerated and produced dose-dependent reductions in levels of mutant huntingtin (mHTT) in the cerebrospinal fluid. Although the trial was not designed to measure efficacy, mHTT lowering was found to correlate with improvements in motor scores and cognitive function.

Richard Finkel provided an update on emerging therapies for spinal muscular atrophy (SMA), including the FDA-approved ASO nusinersen, and gene-replacement strategies. Small-molecule drugs could also have a starring role in the treatment of SMA in the future. Giovanni Baranelli presented data from the FIREFISH Part 1 trial, which tested the small molecule RG7916 in babies with SMA type 2. The drug was found to increase blood levels of survival motor neuron protein (SMN) by modulating *SMN2* gene splicing. Trials are now underway to determine the clinical efficacy of RG7916.

Summarizing the recent therapeutic advances in SMA and other neuromuscular diseases in the final plenary session of the meeting, Ericka Simpson concluded that neuromuscular medicine is reaching a "tipping point", catalysed by a "perfect storm of collaboration".

Heather Wood

PARKINSON DISEASE

Prediction of cognitive decline in PD

Structural and microstructural changes in the nucleus basalis of Meynert are associated with and predictive of cognitive impairment in Parkinson disease (PD), according to a recent study. The work identifies a clinically applicable marker that could help with early identification and treatment of patients at risk.

Cognitive impairment is common in PD, but predictive markers of cognitive decline have not been identified. Loss of cholinergic function has previously been linked to dementia and cognitive impairment, so in their new study, Marios Politis and colleagues focused their attention on the cholinergic nucleus basalis of Meynert.

"Using MRI, we wanted to see whether structural and microstructural changes in the nucleus basalis of Meynert could be underlying cognitive impairment in patients with PD," explains Politis. "We chose MRI because we wanted to use a common imaging technique that is accessible to patients in the clinic."

The researchers analysed data from the Parkinson's Progression Markers Initiative database, including 304 patients with PD and 167 healthy controls. T1-weighted MRI data were used to assess grey matter volume, and diffusion tensor imaging data were used to assess diffusivity in white matter.

Cross-sectional analysis revealed that in patients with PD, cognitive impairment was associated with reduced grey matter volume and increased white matter diffusivity in the nucleus basalis of Meynert. A longitudinal analysis of MRI data, collected over 36 months from patients

PARKINSON DISEASE

Designer exosomes alleviate neurotoxicity

Investigators have developed a cell system that can mass-produce exosomes to shuttle high levels of therapeutic RNA across the blood–brain barrier and into target neurons. Implantation of these cells alleviated neuronal death and neuroinflammation in a mouse model of Parkinson disease (PD), suggesting that this system presents a novel strategy for the treatment of neurological disorders.

Exosomes are small secreted vesicles that mediate communication between cells. These structures have gained increasing attention as a method of delivering targeted therapies, but their short half-life and inefficiency in cargo delivery has limited their use.

"Our laboratory has been focusing on next-generation therapy based on implanted mammalian designer cells," says Martin Fussenegger, corresponding author on the new study. "However, outputs of the cells have been limited to proteins, and therefore we thought there may be some synergistic opportunity of using these two ideas: secreting designer exosomes from implanted cells."

The investigators generated cells that were able to produce neuron-targeted exosomes over a prolonged time frame and could be implanted into living animals. The cells were genetically engineered to boost the efficiency of exosome delivery.

The researchers tested the ability of their system to alleviate neuroinflammation, an important contributing factor in PD. Cells were generated that packaged RNA encoding the antioxidant enzyme catalase, which is